

## AMENDMENTS

### In the Claims:

1. (Currently Amended) A method for determining the predisposition of a subject of Northern European ancestry ~~or non-Northern European ancestry~~ to early-onset menopause, comprising detecting in said subject at least one allele selected from the group consisting of: IL-1RN (+2018) allele 2; ~~and IL-1RN (+2018) allele 1~~, wherein detection of an IL-1RN (+2018) allele 2 in a said subject of ~~Northern European ancestry~~ is predictive of a predisposition to early-onset menopause ~~and wherein detection of an IL-1RN (+2018) allele 1 in a subject of non-Northern European ancestry is predictive of a predisposition to early-onset menopause.~~
- 2.-4. (Cancelled)
5. (Currently Amended) The method of claim 1, wherein detecting said ~~at least one~~ allele comprises allele specific oligonucleotide hybridization.
6. (Currently Amended) The method of claim 1, wherein detecting said ~~at least one~~ allele comprises RFLP analysis.
7. (Currently Amended) The method claim 1, wherein detecting said ~~at least one~~ allele comprises amplification of a nucleic acid.
8. (Currently Amended) The method of claim 7, wherein said amplification ~~further~~ comprises PCR.
9. (Currently Amended) The method of claim 7, wherein said amplification comprises using a first oligonucleotide that overlaps a second oligonucleotide, or a complement thereof, selected from the group consisting of:  
  
5' CTA TCT GAG GAA CAA CCA ACT AGT AGC 3' (SEQ ID NO:7); and  
  
5' TAG GAC ATT GCA CCT AGG GTT TGT 3' (SEQ ID NO:8).
10. (Original) The method of claim 9, wherein said first oligonucleotide comprises at least ten nucleotides of said second oligonucleotide.
- 11.-44. (Cancelled)

## REMARKS

Claims 1 and 5-10 are pending in the application. Claims 1 and 5-9 have been amended herein. The amendment to claim 1 is supported by disclosure at page 61, lines 1-12 of the specification. The amendments to claims 5-9 are merely formalities and are supported by the claims as originally filed. Thus, no new matter has been added.

### **35 U.S.C. § 112, first paragraph**

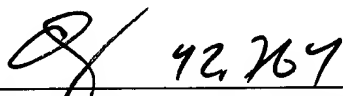
Claims 1, 5-12, 22-24, 43, and 44 were rejected for overbreadth and lack of enablement. The Examiner maintains that while the specification is enabling for methods for determining whether an individual of Northern-European descent is predisposed to early-onset menopause by detecting the presence of IL-1RN (+2018) allele 2 as indicative of a predisposition to early onset menopause, it does not reasonably provide enablement for methods which determine a predisposition to early-onset menopause in non-Northern European women by detecting IL-1RN (+2018) allele 2 or methods for detecting early-onset menopause by detecting any other IL-1 alleles or haplotypes.

Claim 1 has been amended to delete recitation to subjects of non-Northern European ancestry and to delete recitation to detecting IL-1RN (+2018) allele 1. Therefore, amended claim 1 is directed to a method for determining the predisposition of a subject of Northern European ancestry to early-onset menopause by detecting IL-1RN (+2018) allele 2. As mentioned above, the Examiner has acknowledged that the specification is enabling for methods for determining whether an individual of Northern-European descent is predisposed to early-onset menopause by detecting the presence of IL-1RN (+2018) allele 2 as indicative of a predisposition to early onset menopause. Claims 5-10 each depends, either directly or indirectly, from claim 1 and therefore necessarily contains all of the limitations of claim 1. Claims 11-12, 22-24, 43, and 44 have been cancelled. Thus, Applicants request that this rejection be withdrawn.

**CONCLUSION**

On the basis of the foregoing amendments, Applicants respectfully submit that the pending claims are in condition for allowance, and a Notice of Allowance is respectfully requested. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

  
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